Susceptibilities of 45 Clinical Isolates of Proteus penneri

MILAN FUKSA, 1* SIGMUND KRAJDEN, 2 AND ALBERT LEE1

Department of Microbiology, St. Joseph's Health Center, Toronto, Ontario M6R 1B5, and Department of Microbiology, Faculty of Medicine, University of Toronto, Toronto, Ontario M5G 1L5, Canada

Received 19 June 1984/Accepted 26 June 1984

Patterns of susceptibility of 45 *Proteus penneri* clinical isolates to 14 antimicrobial agents were evaluated by a macrobroth dilution method. All strains were highly susceptible to ceftizoxime, ceftazidime, moxalactam, cefoxitin, gentamicin, tobramycin, netilmicin, and, with few exceptions, to amikacin, piperacillin, and cefoperazone. Most strains were susceptible to cefotaxime and ceftriaxone. All strains were resistant to cefazolin and cefsulodin.

Proteus penneri has been recently recognized as a new member of the tribe Proteeae (4, 12). Previously, it had been classified as indole-negative P. vulgaris biogroup 1. P. penneri is indole, esculin, and salicin negative after 48 h of incubation and exhibits a narrow zone of inhibition around a 30-µg chloramphenicol disk (usually <14 mm). These characteristics are essential in differentiating P. penneri from P. vulgaris biogroup 2 (indole, salicin, and esculin positive, chloramphenicol susceptible) and from P. vulgaris biogroup 3 (indole positive, salicin and esculin negative). The chloramphenicol resistance pattern of the latter biogroup has not yet been satisfactorily delineated (4).

P. penneri has been isolated from urine, blood, stools, abdominal wounds, and bronchial exudates (4); however, its natural habitat is unknown, and its etiological role in infectious processes has not been fully established. One recent report implicated P. penneri in a urinary tract infection with bladder calculi formation (10).

A total of 45 clinical isolates of *P. penneri* were included in the study. Forty isolates, including the type strain ATCC 33519, were supplied by the University of Toronto, Toronto Ontario, Canada (courtesy of J. L. Penner), and five strains were isolated from patients at St. Joseph's Health Center, Toronto, Ontario, Canada. Isolates were identified by standard criteria (4).

MICs of the following antimicrobial agents were determined by the macrobroth dilution method (21): cefazolin (Smith Kline & French Canada, Inc.), cefotaxime (Roussel Canada, Inc.), cefoxitin (Charles Frosst & Co., Canada), ceftazidime (Glaxo Canada, Ltd.), ceftizoxime (Smith Kline & French Canada, Inc.), ceftriaxone (Hoffmann-La Roche, Ltd.), cefoperazone (Pfizer Canada, Inc.), cefsulodin (Ciba-Geigy Canada, Inc.), moxalactam (Eli Lilly & Co. of Canada), piperacillin (Cyanamid Canada, Inc.), gentamicin (Schering Corp.), tobramycin (Eli Lilly & Co. of Canada), netilmicin (Schering Canada, Inc.), and amikacin (Bristol Laboratories of Canada).

The activities of individual antimicrobial agents against clinical isolates of P. penneri are shown in Table 1. A total of 90% of isolates were inhibited by (per milliliter) 0.25 μ g of ceftizoxime, 0.5 μ g of ceftazidime and moxalactam, 1 μ g of gentamicin, 2 μ g of tobramycin, and 4 μ g of netilmicin and cefoxitin. The least active agents against P. penneri were cefsulodin and cefazolin, with MICs for 90% of the isolates (MIC₉₀s) of >128 μ g/ml. According to the MIC interpretative standards outlined by Washington and Sutter (21), Thornsberry et al. (19), and the drug company information

brochures, *P. penneri* strains were 100% susceptible to ceftizoxime, ceftazidime, moxalactam, cefoxitin, gentamicin, tobramycin, and netilmicin, 97.8% susceptible to amikacin, 95.6% susceptible to piperacillin and cefoperazone, 84.4% susceptible to cefotaxime, 64.4% susceptible to ceftriaxone, and 0% susceptible to cefsulodin and cefazolin. Furthermore, in standard disk diffusion tests (2), it was found that 94.9% (37 of 39) of isolates were susceptible to nalidixic acid and 61.5% (24 of 39) of isolates were susceptible to nitrofurantoin.

When our results were compared with those reported by others for P. vulgaris, it was evident that there were considerable similarities in susceptibilities to cefazolin (1, 8, 9, 18, 20), moxalactam (1, 5, 7, 11, 14, 16, 20), tobramycin (5, 7), amikacin (5, 15), and ceftazidime (13, 14, 22). P. penneri appears to be more resistant to ceftriaxone than does P. vulgaris with MIC₉₀s of 64 and 0.12 to 12.5 μg/ml, respectively (1, 13, 17, 22). Whereas P. penneri was generally resistant to cefoperazone (MIC₉₀, 32 μ g/ml), P. vulgaris strains have been reported to have MIC₉₀s as low as 1 µg/ml and as high as $100 \mu g/ml$ (1, 5, 6, 13, 14, 18). There appears to be a marked susceptibility of P. penneri to ceftizoxime (MIC₉₀, 0.25 μg/ml), in contrast to P. vulgaris (MIC₉₀s, 2 and 12.5 μg/ml [references 13 and 17, respectively]). Cefoxitin was only slightly more active against P. penneri (MIC₉₀, 4 μ g/ml) than against P. vulgaris (MIC₉₀s, 6.25, 8, 16, 32, and 50 μg/ml [references 1, 5, 9, 13, and 18, respectively]). In a recent report, P. penneri strains were reported to be more

TABLE 1. Comparative MICs (micrograms per milliliter) of 14 antimicrobial agents against 45 strains of *P. penneri*

Antibiotic	MIC range	Modal MIC	MIC ₅₀ ^a	MIC ₉₀
Cefotaxime	≤0.12-≥32	1	1	>16
Cefoperazone	≤1 - 128	1	2	32
Ceftriaxone	0.12 -> 128	0.5	1	64
Ceftazidime	0.06-2	0.12	0.12	0.5
Cefazolin	≥128	>128	>128	>128
Cefoxitin	1-8	4	2	4
Cefsulodin	≤64->128	128	128	>128
Ceftizoxime	≤0.03-2	≤0.03	0.03	0.25
Moxalactam	≤0.25 - 2	≤0.25	0.25	0.5
Piperacillin	≤1-≥128	≤1	2	16
Gentamicin	0.5-4	1	0.5	1
Tobramycin	0.25-8	2	1	2
Netilmicin	0.5-8	2	2	4
Amikacin	1-32	8	4	8

^a MIC₅₀, MIC at which 50% of the isolates were inhibited.

^{*} Corresponding author.

resistant to the newer semisynthetic ureidopenicillins, azlocillin and mezlocillin (3). However, in our study, *P. penneri* strains were generally found to be susceptible to piperacillin (MIC₉₀, 16 µg/ml). Although the patterns of susceptibility to these three ureidopenicillins, ceftizoxime, and ceftriaxone suggest a basis for differentiating *P. penneri* from *P. vulgaris*, more isolates need to be studied.

420

The overall evaluation of the in vitro activity of ceftizoxime, ceftazidime, moxalactam, and cefoxitin suggests that these agents may prove to be clinically useful in treating infections caused by *P. penneri*. All four aminoglycosides tested were extremely active against *P. penneri* and should therefore be considered as drugs of choice for the treatment of systemic infections caused by susceptible *P. penneri* strains.

We thank J. L. Penner for supplying clinical isolates and critically reviewing the manuscript, A. Guia and M. Javier for technical assistance, and P. Catterall for typing the manuscript.

This study was supported by a grant from Eli Lilly & Co. of Canada.

LITERATURE CITED

- Ayers, L. W., R. N. Jones, A. L. Barry, C. Thornsberry, P. C. Fuchs, T. L. Gavan, E. H. Gerlach, and H. M. Sommers. 1982. Cefotetan, a new cephamycin: comparison of in vitro antimicrobial activity with other cephems, β-lactamase stability, and preliminary recommendations for disk diffusion testing. Antimicrob. Agents Chemother. 22:859–877.
- Barry, A. L., and C. Thornsberry. 1980. Susceptibility testing: diffusion test procedures, p. 463-474. In E. H. Lennette, A. Balows, W. J. Hausler, Jr., and J. P. Truant (ed.), Manual of clinical microbiology, 3rd ed. American Society for Microbiology, Washington, D.C.
- Hawkey, P. M., S. J. Pedler, and A. Turner. 1983. Comparative in vitro activity of semisynthetic penicillins against *Proteeae*. Antimicrob. Agents Chemother. 23:619-621.
- Hickman, F. W., A. G. Steigerwalt, J. J. Farmer III, and D. J. Brenner. 1982. Identification of *Proteus penneri* sp. nov., formerly known as *Proteus vulgaris* indole negative or as *Proteus vulgaris* biogroup 1. J. Clin. Microbiol. 15:1097-1102.
- Jacobus, N. V., M. C. Ferreira, and M. Barza. 1982. In vitro activity of azthreonam, a monobactam antibiotic. Antimicrob. Agents Chemother. 22:832-838.
- Jones, R. N., and A. L. Barry. 1983. Antimicrobial activity and other in vitro properties of cefoperazone A, the principal metabolite of cefoperazone sodium. Antimicrob. Agents Chemother. 24:293-296.
- Jones, R. N., P. C. Fuchs, H. M. Sommers, T. L. Gavan, A. L. Barry, and E. H. Gerlach. 1980. Moxalactam (LY127935), a new semisynthetic 1-oxa-β-lactam antibiotic with remarkable antimicrobial activity: in vitro comparison with cefamandole and tobramycin. Antimicrob. Agents Chemother. 17:750-756.
- 8. Kato, M., M. Inoue, and S. Mitsuhashi. 1982. Antibacterial

- activities of SM-1652 compared with those of other broadspectrum cephalosporins. Antimicrob. Agents Chemother. 22:721-727.
- Kobayashi, F., Y. Saino, T. Koshi, Y. Hattori, M. Nakayama, A. Iwasaki, T. Mori, and S. Mitsuhashi. 1982. Antimicrobial and β-lactamase inhibitory activities of carpetimycins A and B, new carbapenem antibiotics. Antimicrob. Agents Chemother. 21:536-544.
- Krajden, S., M. Fuksa, W. Lizewski, L. Barton, and A. Lee. 1984. Proteus penneri and urinary calculi formation. J. Clin. Microbiol. 19:541-542.
- Kurtz, T. O., D. J. Winston, W. J. Martin, L. S. Young, and W. L. Hewitt. 1980. Comparative in vitro activity of moxalactam (LY127935), other beta-lactam antibiotics, and aminoglycosides. Curr. Microbiol. 4:21-26.
- List no. 11. 1983. Validation of the publication of new names and new combinations previously effectively published outside the IJSB. Int. J. Syst. Bacteriol. 33:672-674.
- Muytjens, H. L., and J. van der Ros-van de Repe. 1982.
 Comparative activities of 13 β-lactam antibiotics. Antimicrob.
 Agents Chemother. 21:925-934.
- Neu, H. C., and P. Labthavikul. 1983. In vitro activity and β-lactamase stability of U-63196E, a novel cephalosporin. Antimicrob. Agents Chemother. 24:375-382.
- Penner, J. L., M. A. Preston, J. N. Hennessy, L. J. Barton, and M. M. Goodbody. 1982. Species differences in susceptibilities of Proteeae spp. to six cephalosporins and three aminoglycosides. Antimicrob. Agents Chemother. 22:218-221.
- Schell, R. F., B. R. Smith, J. L. LeFrock, and M. Francisco. 1983. Antimicrobial activity of cefmenoxime compared with those of other cephalosporins. Antimicrob. Agents Chemother. 23:774-777.
- Scully, B. E., K. Jules, and H. C. Neu. 1983. In vitro activity and β-lactamase stability of cefodizime, an aminothiazolyl iminomethoxy cephalosporin. Antimicrob. Agents Chemother. 23:907-913.
- Tai, M., Y. Fukuoka, A. Yotsuji, K. Kumano, M. Takahata, H. Mikami, T. Yasuda, I. Saikawa, and S. Mitsuhashi. 1982. In vitro and in vivo antibacterial activity of T-1982, a new semisynthetic cephamycin antibiotic. Antimicrob. Agents Chemother. 22:728-724
- Thornsberry, C., T. L. Gavan, J. C. Sherris, A. Balows, J. M. Matsen, L. D. Sabath, F. Schoenknecht, L. D. Thrupp, and J. A. Washington II. 1975. Laboratory evaluation of a rapid, automated susceptibility testing system: report of a collaborative study. Antimicrob. Agents Chemother. 7:466-480.
- Verbist, L. 1982. In vitro activity of temocillin (BRL 17421), a novel beta-lactamase-stable penicillin. Antimicrob. Agents Chemother. 22:157-161.
- Washington, J. A., II, and V. L. Sutter. 1980. Dilution susceptibility test: agar and macro-broth dilution procedures, p. 453–458. In E. H. Lennette, A. Balows, W. J. Hausler, Jr., and J. P. Truant (ed.), Manual of clinical microbiology, 3rd ed. American Society for Microbiology, Washington, D.C.
- Wise, R., J. M. Andrews, and G. Danks. 1983. Comparison of in vitro activity of FCE 22101, a new penem, with those of other βlactam antibiotics. Antimicrob. Agents Chemother. 24:909-914.